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New chiral pyridino-18-crown-6 ligands containing two amide, thionoamide or amine units and two benzyl or phenyl substituents on chiral macroring positions have been synthesized (see Figure 1). Some of these chiral ligands exhibit only moderate or no recognition for the enantiomers of [α-(1-naphthyl)ethyl]ammonium perchlorate as determined by ^{1}H NMR spectral techniques.

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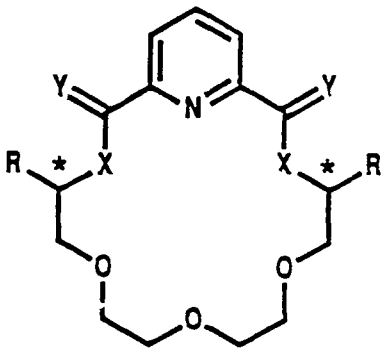
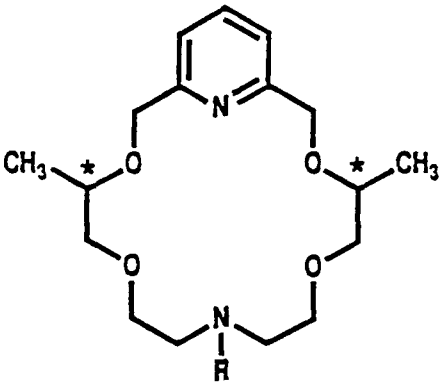
Figure 1. Chiral Diamido-, Dithionoamido-, Diaza- and Azapyridino-18-crown-6 Ligands





1, X = NH; Y = O; R = benzyl (*S,S*)
2, X = NH; Y = S; R = benzyl (*S,S*)
3, X = NH; Y = H_2; R = benzyl (*S,S*)
4, X = NH; Y = O; R = phenyl (*S,S*)
5, X = NH; Y = S; R = phenyl (*S,S*)
6, X = NH; Y = H_2; R = phenyl (*S,S*)
7, X = NCH_3; Y = O; R = phenyl (*S,S*)
8, X = NCH_3; Y = S; R = phenyl (*S,S*)
9, X = NCH_3; Y = H_2; R = phenyl (*S,S*)

10, R = H (*S,S*)
11, R = $C(O)CH_3$ (*S,S*)

Complexation of the enantiomeric forms of NapEt by some of the new ligands has been studied by the temperature-dependent ^1H NMR technique[1-5], and by determining the log *K* values for the association of the chiral ligand and the enantiomer salt by a direct ^1H NMR spectral method.[5,9] Table I contains the free energy of activation ($\Delta G_c^{\ddagger}$) and log *K* values for the interaction of some of these new chiral ligands with the enantiomers of [α-(1-naphthyl)ethyl]ammonium perchlorate(NapEt). The data show that, in general, these chiral ligands exhibit only moderate or no recognition for the enantiomers of NapEt. The $\Delta G_c^{\ddagger}$ data show that ligands **7**, **8**, and **9** form stable

complexes in CD_2Cl_2 with the (*R*) and (*S*) forms of NapEt but the resulting complexes each have about the same kinetic stability. This is in sharp contrast to complexation by the chiral diphenyl-substituted pyridino-18-crown-6 (Y = H_2, X = O, R = phenyl) and diesterpyridino-18-crown-6 (Y = O, X = O, R = phenyl) ligands (see Figure 1) which exhibited considerable recognition of one form of NapEt over the other form in CD_2Cl_2 as determined by the temperature dependent ^1H NMR method.[5] Log *K* values in Table I do show that some of these ligands exhibit enantiomeric recognition in a mixture of 50% $CDCl_3$ - 50% CD_3OD or in CD_3NO_2. Dithionoamide (*S*,*S*)-5 favored (*R*)-NapEt over (*S*)-NapEt by 0.37 log *K* units. This recognition compares favorably with that obtained by the similar diphenyl-substituted crown (X = O, Y = O) ligand.[5] Ligand (*S*,*S*)-8 also exhibited moderate recognition for ?)-NapEt in the 50% $CDCl_3$ - 50% CD_3OD mixture. Ligands (*S*,*S*)-1 and (*S*,*S*)-7 exhibit some recognition for one form of NapEt in CD_3NO_2. Thus, in some cases, these new chiral ligands show moderate enantiomeric recognition but they have inferior recognition properties as compared to the diphenyl- and di-t-butyl-substituted pyridino- and diesterpyridino-18-crown-6 ligands (all have X = O).[5]

The data in Table I also show that log *K* values for macrocycle-ammonium salt interactions increase as the polarity of the solvent decreases. This is an expected trend for solvent effects in these types of interactions. It is also instructive to note that there is a significant decrease in log *K* values when substituting an amide group for an ester in these systems. This is best observed by comparing the log *K* value of 0.7 (Table 1) for the interaction of (*S*,*S*)-4 with (*R*)-

NapEt in a mixture of 50% $CDCl_3$ - 50% CD_3OD with a log *K* value of 2.15 for the same interaction of the comparable ester (X and Y = O, R = phenyl) in a mixture of 30% $CDCl_3$ - 70% CD_3OD.[5] The two solvent systems are slightly different but the latter solvent is more polar which should decrease the log *K* value. This significant decrease in complexing ability for the diamido-crowns is probably a result of distorted macrorings that will be mentioned later. The diamino-crowns, on the other hand, form stronger complexes as shown by the log *K* value of 3.2 for the interaction of (*S*,*S*)-9 with (*R*)-NapEt.

Table I. Free Energies of Activation ($\Delta G_c^{\ddagger}$)[a] and log K Values[b] for the Interaction of Some Chiral Macrocyclic Ligands with the R and S Forms of [α-(1-Naphthyl)ethyl]ammonium Perchlorate (NapEt)

Ligand	$\Delta G_c^{\ddagger}$ values (Kcal/mol)[c]		log K values at 20 °C			
	(R)-NapEt	(S)-NapEt	(R)-NapEt[d]	(S)-NapEt[d]	(R)-NapEt[e]	(S)-NapEt[e]
(S,S)-1			g	g	0.8	1.00
(S,S)-4	f	f	0.7	g		
(S,S)-5			1.39	1.02		
(S,S)-7	11.3	11.2	g	g	2.75	2.55
(S,S)-8	>14.0	>13.9	0.7	0.5		
(S,S)-9	12.0	12.1	3.2	3.3	h	h

[a] A Varian VXR-500 spectrometer was used to record all ^1H NMR Spectra for determination of both $\Delta G_c^{\ddagger}$ and log K values. The procedure for the determination of $\Delta G_c^{\ddagger}$ values was as described in ref. 1-5.

[b] Log K values were determined by a direct ^1H NMR procedure as described in ref. 9.

[c] CD_2Cl_2 was used as a solvent.

[d] 50%/50% (v/v) $CDCl_3$-CD_3OD mixture was used as a solvent.

[e] CD_3NO_2 was used as a solvent.

[f] No splitting was observed in the ^1H NMR spectra.

[g] Log K value was so low that accurate measurements could not be made.

[h] Log K value was so high that accurate calculations could not be made.

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